Remarks

Claims 1-25, 27-32, 34-36 and 61 are presently pending in the subject application.

Reconsideration and allowance in view of the above amendments and the following remarks are respectfully requested.

The specification and claim 36 have been amended herein in the manner described below.

Objections to the Specification

The Examiner objects to Applicant's incorporation by reference of entire documents in the specification on the grounds that Applicant has not indicated why the referenced documents are being incorporated and that Applicant has not identified which portions of the documents are considered to be relevant. In response, Applicant first observes that there is no affirmative duty to state in a specification, as the Examiner suggests, why a particular documented is being incorporated by reference. *See* MPEP § 608.01(p) at 600-82 (8th ed., Rev. 2, May 2004). Second, Applicant submits that there is no obligation to point to the relevant portions of a document when an applicant believes, and the context suggests, that the referenced document as a whole is relevant. In the present case, Applicant has incorporated by reference, *inter alia*, documents which disclose methods for extracting nucleic acids for use in detection assays, different types of amplification procedures, methods and means for detecting nucleic acids, and particular kinds of nucleic acid analogs. The referenced documents provide information such as compositions, processes, reagents and conditions. Thus, given the context of each incorporation by reference in the specification, Applicant submits that those skilled in the art would readily appreciate the relevance of incorporated documents in their entireties. Therefore, if this rejection is to be maintained, then Applicant requests that the Examiner state with particularity why each incorporated document should be limited to a particular section and what section of each such document the Examiner believes the disclosure should be limited to.

Applicant's Reply filed on August 26, 2004 is objected to by the Examiner for introducing new matter into the disclosure. In support of this objection, the Examiner first argues that the insertion of language in the specification that various documents have been incorporated by reference constitutes new matter. This is not the case since Applicant's specification, as filed, incorporated all documents referred to in the specification by reference in their entireties. *See* specification at page 1, lines 15-16. Thus, to now limit those documents incorporated by reference to a subset of those originally incorporated by reference cannot constitute new matter.

Second, the Examiner objects to the substitution of U.S. patent applications [*sic*, U.S. patents] for foreign applications in Applicant's prior Reply. To clarify, in those instances where an international application was listed in combination with a U.S. application, the reference to the U.S. application was substituted with a reference to the U.S. patent that issued directly therefrom and the reference to the international application was simply deleted. In one case, there was a reference to an international application that was substituted with a reference to a corresponding U.S. patent. Rather than filing a declaration or affidavit in support of this latter change to the specification, Applicant has elected to amend the specification to re-identify the international application that was previously deleted. *See* amendment to the paragraph bridging pages 10 and 11 of the specification.

Finally, Applicant's prior Reply amended page 4, lines 15-16, of the specification to indicate that the polynucleotide probes of the claimed invention have net "negative" charge rather than a net "positive" charge, as Applicant inadvertently stated in the originally filed application. In objecting to this amendment, the Examiner seems to assert that Applicant's disclosure provides that the polynucleotides bind to the polycations to form a complex that is negatively charged rather than that the polynucleotides alone are negatively charged. The Examiner's conclusion is in discord with the clear teaching of the specification, which provides as follows:

> . . . the applicant currently believes that the polycationic polymers of the present invention assemble in solution to form complexes of nanometer dimensions (*i.e.*, nonoparticles) which create a charge environment that attracts negatively charged polynucleotides (*e.g.*, polynucleotide probes and target nucleic acids) present in the solution.

See specification at paragraph bridging pages 29 and 30 (emphasis added). Thus, Applicant's disclosure makes it is indisputable that the polynucleotides of the claimed invention must be negatively charged. Moreover, contrary to the Examiner's reading of the description, the section of the specification where the inadvertent error occurred is limited to a discussion of polynucleotides useful in the present invention and not to a complex made up of both polynucleotides and polycations. *See* specification at page 4, lines 14-25. In this section of the specification, Applicant also discloses that the polynucleotides must have anionic groups and may consist of RNA or DNA. And if, as disclosed, a polynucleotide may consist of RNA or DNA, then it cannot have a net positive charge. Therefore, Applicant's submit that use of the phrase "net positive charge" was a clear error that would have been readily recognized by those having ordinary skill in the art.

For the reasons provided above, Applicant respectfully requests withdrawal of the Examiner's objections to the specification.

Objection to the Claims

Claim 36 is objected to by the Examiner under 37 C.F.R. § 1.75(c) as being of improper dependent form. In response, Applicant has amended claim 36 herein to depend from claim 1. Accordingly, withdrawal of the Examiner's objection to claim 36 is respectfully requested.

Rejections Under 35 U.S.C. § 112

Claims 1-25, 27-32, 34-36 and 61 stand rejected by the Examiner under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. Applicant respectfully traverses this rejection for the reasons that follow.

Under this rejection, the Examiner first argues that claim 1 covers "simultaneous detection of an infinite number of target nucleic acids." First, assuming *arguendo* that the Examiner's assertion is true, the Examiner has failed to state why the detection of multiple target nucleic acids would raise a written description issue since the stated objective of the claim is to detect target nucleic acid. (An example of multiple target nucleic acids contemplated by the claims is extracted nucleic acid and a nucleic acid amplification product thereof, where the extracted nucleic acid and the amplification product contain the same target nucleic acid sequence, excluding RNA and DNA equivalents.) Second, the Examiner has made no attempt to explain what this potentially "infinite" set of target nucleic acids would be comprised of and how this potentially infinite set of target nucleic acids would wind-up in the sample being interrogated. Third, Applicant submits that this rejection fails to take into consideration all the limitations of the claim, as the claim specifically recites that the probe will "preferentially hybridize" to the target nucleic acid, thereby indicating the presence of a specific target nucleic acid sequence. *See, e.g.*, specification at page 13, line 3 *et seq.*

The Examiner states that the examples are limited to experiments involving just six different polycationic polymers. Applicant is unaware, however, of any obligation to provide examples to satisfy the written description requirement, and the Examiner has failed to identify any such obligation. Additionally, the Examiner's statement that Applicant has exemplified a limited number of polycationic polymers is not evidence or reasoning that Applicant has failed to adequately describe the claimed invention. Also, the specification goes to great lengths to describe the features of polycationic polymers that can be used in the claimed method. *See, e.g.*, specification page 27, line 24 *et seq.* Therefore, if this rejection is to be maintained, then evidence or reasoning in support thereof is respectfully requested. *See* MPEP § 2163.04 at 2100-173 (8th ed., Rev. Feb. 2003).

It is further argued by the Examiner that step b) of claim 1 only requires that the reactants be exposed to a "dissociation [*sic*, dissociating] reagent in amount sufficient to dissociate said polymer from said duplex." This is true, but only in part. Step b) of claim 1 further requires

that the sample be exposed to the dissociating reagent after the probe and target nucleic acid have had sufficient time to associate in the sample, thereby excluding reagents present in the sample before the probe and target nucleic acid have had sufficient time to associate. Examples of dissociating reagents are provided in the specification at page 7, lines 5-11, and page 37, lines 25-26.

The Examiner further contends that the claims do not require that the dissociating reagent be provided under conditions that will result in dissociation, nor do the claims require that any dissociation take place. As noted by the Examiner, the claims require that the sample be exposed to a dissociating reagent "in an amount sufficient to dissociate said polymer from said duplex." Thus, if the conditions of an assay are such that dissociation of the polymer from the probe:target nucleic acid duplex cannot take place, then the dissociating reagent has not been provided to the sample in an amount sufficient to dissociate the polymer from the probe:target nucleic acid duplex and this limitation of the claim has not been satisfied. Furthermore, a reason that the claim does not require that dissociation occur is because the claim does not require that the target nucleic acid even be present in the sample, as the claims are directed to a method for determining whether the target nucleic acid is present in the sample.

The Examiner concludes this rejection by suggesting that Applicant is attempting to satisfy the written description requirement through obviousness. But this conclusion is unsupported by any facts, especially by any references to statements made on the record by Applicant. Since the Examiner has not provided Applicant with any basis for responding to this argument, and Applicant has been diligent to respond to all of the Examiner's rejections with references to the description, no response can be made to the Examiner's contention without engaging in conjecture.

Based on the foregoing, Applicant submits that the written description requirement has been satisfied and, therefore, withdrawal of the Examiner's written description rejection under 35 U.S.C. § 112, first paragraph, is respectfully requested.

Claims 1-25, 27-32, 34-36 and 61 stand rejected by the Examiner under 35 U.S.C. § 112, first paragraph, as failing to comply with the enablement requirement. Applicant respectfully traverses this rejection for the reasons that follow.

The Examiner states that claim 1 encompasses the detection of any number of different target polynucleotides with any one or more probes in a simultaneous manner where no label or detection means is employed. From this statement, it is difficult to ascertain the exact basis or bases for the Examiner's rejection. Nevertheless, the Examiner is first directed to Applicant's response to the written description rejection above, where the importance of the probe's claimed ability to preferentially hybridize to the target nucleic acid is discussed. Further, while it is true that claim 1 does not specify a label, Applicant wishes to point out that detection means are available, and well known in the art, that do not require the presence of a label for detection of a probe hybridized to a target nucleic acid. *See, e.g.*, specification at page 17, lines 4-12. Finally, Applicant has disclosed a number of non-limiting labels for detecting probes hybridized to target nucleic acids (*see, e.g.*, specification at page 27, lines 3-22), heterogenous and homogenous systems that are well known in the art (*see, e.g.*, specification at page 35, line 24 *et seq.*), as well as instrument systems for performing detection assays (*see, e.g.*, specification at page 40, lines 4-18).

The Examiner contends that the claimed method encompasses performing all the steps with the reactants in solution and no apparent means for retaining the duplex should one reactant be removed from the solution. It would appear that the Examiner is arguing that Applicant's claims cover both heterogenous and homogenous assays. As noted above, both types of assays are described in the specification at, for example, page 35, line 24 *et seq.* The contents of the documents cited in this section of the specification are all incorporated by reference in their entireties.

The Examiner also contends that the phrase "forming a duplex" in the claims encompasses both duplex and triplex structures. This interpretation of the term "duplex," however,

is contradicted by Applicant's definition, which provides that a "duplex" is a stable nucleic acid structure comprising a double-stranded, hydrogen-bonded region. *See* specification at page 17, lines 1-4. Thus, the claims require that the probe and the target nucleic acid form a double-stranded bond, or duplex, rather than a triplex structure. And even if triplex structures were covered by the claims, the Examiner has failed to explain why the enablement requirement is not satisfied by Applicant's disclosure. Therefore, if this rejection is to be maintained, then evidence or reasoning in support thereof is respectfully requested. *See* MPEP § 2163.04 at 2100-173 (8th ed., Rev. Feb. 2003).

The Examiner submits that the clause "in an amount sufficient to increase the association rate of said probe an [*sic,* and] said target nucleic acid" encompasses "values that both allow for an [*sic*, and] exceed this increased rate of association." As stated, Applicant is unable to determine what the basis is for the Examiner's rejection. The claims specify that the presence of the polycationic polymer in the sample increases the rate at which the polynucleotide probe and the target nucleic acid associate. If the claims require an increased rate of association, as they do, then it is unclear how the claim can be interpreted to also cover values which "exceed this increased rate of association." Put another way, if the claim specifies an increased rate of association, then there is no value that could exceed this increased rate of association since no upper limit is specified. Therefore, if this rejection is to be maintained, then evidence or reasoning in support thereof is respectfully requested. *See* MPEP § 2163.04 at 2100-173 (8th ed., Rev. Feb. 2003).

The Examiner further submits that the phrase "polycationic polymer" encompasses both organic and inorganic polycationic polymers, exhibiting a range of hydrophobicity and hydrophilicity, and can have virtually any upper mass. This, however, is not evidence or reasoning that Applicant has failed to adequately enable the claimed invention. Moreover, the specification goes to great lengths to describe the features of polycationic polymers that can be used in the claimed method. *See, e.g.,* specification at page 6, lines 21-26, and page 27, line 24 *et seq.* Therefore, if this

rejection is to be maintained, then evidence or reasoning in support thereof is respectfully requested. *See* MPEP § 2163.04 at 2100-173 (8th ed., Rev. Feb. 2003).

The Examiner correctly observes that the claims require conditions such that the probe preferentially hybridizes to the target nucleic acid. Yet, the Examiner goes on to state, without any evidence or reasoning, that such language encompasses "the formation of duplex structures with non-target sequences in nearly equal amounts." As Applicant has previously stressed, the Examiner's interpretation is directly contradicted by the definitions section of the application, where the phrase "preferentially hybridize" is defined to mean "that under the specified hybridization assay conditions, polynucleotide probes can hybridize to their target nucleic acids to form stable probe:target hybrids indicating the presence of a specific target nucleic acid sequence, and there is not formed a sufficient number of stable probe:non-target hybrids to indicate the presence of non-target nucleic acids." *See* specification at page 13, lines 3-15 (emphasis added). If this rejection is to be maintained, then Applicant respectfully requests that the Examiner's conclusion be properly supported with evidence or reasoning. *See* MPEP § 2163.04 at 2100-173 (8th ed., Rev. Feb. 2003).

The Examiner urges that the examples provided in the specification do not fully enable the claimed invention. Similar to Applicant's response to the Examiner's written description rejection, Applicant submits that a limited number of examples is not, standing alone, evidence or reasoning that Applicant has failed to fully enable the claimed invention. Further, in addition to the examples, the specification goes to great lengths to describe the features of polycationic polymers that can be used in the claimed method. *See, e.g.,* specification at page 6, lines 21-26, and page 27, line 24 *et seq*. Therefore, if this rejection is to be maintained, then evidence or reasoning in support thereof is respectfully requested. *See* MPEP § 2163.04 at 2100-173 (8th ed., Rev. Feb. 2003).

Finally, based on the arguments in support of the written description rejection, the Examiner concludes that Applicant cannot enable that which he did not possess at the time the

instant application was filed. For the reasons set forth above, Applicant submits the written description clearly demonstrates that he was in possession of the claimed invention at the time the instant application was filed and, accordingly, that the claimed invention is fully enabled.

Based on the foregoing, Applicant submits that the presently claimed invention is fully enabled and, therefore, withdrawal of the Examiner's enablement rejection under 35 U.S.C. § 112, first paragraph, is respectfully requested.

Claims 1-25, 27-32, 34-36 and 61 stand rejected by the Examiner under 35 U.S.C. § 112, second paragraph, as failing to set forth the subject matter which Applicant regards as his invention. Applicant respectfully traverses this rejection for the reasons that follow.

The Examiner contends that the presently pending claims do not correspond in scope with that which Applicant regards as the invention. To support this contention, the Examiner points to the "Field of the Invention" section of the specification and to the originally filed claims. In particular, the Examiner contends that the claims are now drawn to a method of determining the presence of a target nucleic acid. This rejection is not understood, as Applicant's original claim 33 recited determining whether the duplex has formed in the sample. (The limitation of former claim 33 was incorporated into claim 1 in Applicant's prior Reply.) Additionally, the specification very clearly discloses detecting the formation of probe:target nucleic acid duplexes. *See, e.g.*, the specification at page 4, lines 4-13, and the paragraph bridging pages 5 and 6. The specification also contemplates detecting the presence or amount of probe bound to a target nucleic acid. *See, e.g.*, the specification at page 35, lines 24-27. Accordingly, Applicant submits that the claims correspond in scope with the disclosure and, therefore, withdrawal of this rejection is respectfully requested.

Conclusion

Applicant submits that the claims are in condition for allowance and notice to that effect is earnestly solicited.

No fee is believed due in connection with this Amendment. If Applicant is mistaken, please charge the amount due to Deposit Account No. 07-0835 in the name of Gen-Probe Incorporated.

Certificate of Transmission

I hereby certify that this correspondence (and any referred to as attached) is being sent by facsimile to 703-872-9306 on the date indicated below to the Mail Stop AF, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

Respectfully submitted,

Date: January 24, 2005

By: _____

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